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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,989	03/23/2001	Alexander Gad	60807-A-PCT-US/JPW/GJG	7587

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Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 09/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/816,989	GAD ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *123-125,127 and 129-166* is/are pending in the application.

4a) Of the above claim(s) *143* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *123-125, 127, 129-142, and 144-166* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 123-125, 127, and 129-166 are pending.

2. Claim 143 stands withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 123-125, 127, 129-142 and 144-169 are being acted upon in this Office Action.

4. It is noted that Exhibits 6 through 14 and a copy of 1449 enclosed in the amendment filed 6/27/03 are missing.

5. In view of the amendment filed 6/27/03, the following rejections remain.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 123-125, 127, 129-142, and 144-166 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method for treating an autoimmune disease wherein the autoimmune disease is multiple sclerosis in a mammal comprising administering the mammal a purified polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and 7, **does not** reasonably provide enablement for (1) a method of treating *any* autoimmune disease, *any* B cell mediated autoimmune disease, or *any* T cell mediated autoimmune disease or any autoimmune disease such as the ones recited in claims 134 and 144, *any* graft versus host disease, *any* host versus graft disease, or *any* delayed type hypersensitivity in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7 or a mixture of purified polypeptides as set forth in claims 123-142, and 144-151; (2) a method of delaying the onset of any autoimmune disease, *any* B cell mediated autoimmune disease, or *any* T cell mediated autoimmune disease or any autoimmune disease such as the ones recited in claim 158, *any* graft versus host disease, *any* host versus graft disease, or *any* delayed

type hypersensitivity in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7 or a mixture of purified polypeptides as set forth in claims 152-166. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method for treating female (SJL/J x BALB/c) mice with mouse spinal cord homogenate to induce EAE, which is a autoimmune model for multiple sclerosis and a polypeptide selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7. The results show in Table 14 that only polypeptides SEQ ID NO: 2, and 7 block the progression of EAE while treatment with polypeptides of SEQ ID NO: 4, 5 and 6 fail to block the progression of EAE (see page 38). In fact, treatment with polypeptides of SEQ ID NO: 4-6 does not prevent EAE because it has a mean onset of EAE at days 11.7, 14, and 12, respectively, as compared to control (11.3 days). The delayed onset of disease for polypeptides of SEQ ID NO: 4 and 6 (11.7 and 12.0 days, respectively) is not significantly different than the control (11.3 days). Note, the block in the progression of disease is the treatment using polypeptides of SE QIDNO: 2 and 7 could simply due to a delay in the onset of EAE because there is insufficient information on the time course in the specification as filed, much less about relapse.

The specification does not teach a method of treating *any* autoimmune disease mentioned above because of the following reasons:

(1) There is insufficient guidance and in vivo working examples demonstrating that the claimed method of using any polypeptides mentioned above could treat any autoimmune disease such as *any* B cell mediated autoimmune disease, *any* T cell mediated autoimmune disease, *any* demyelinating disease, *any* inflammatory disease, any autoimmune disease such as rheumatoid

arthritis, osteoarthritis, multiple sclerosis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, much less Graft versus host disease, Host versus Graft disease associated with transplant or any delayed type hypersensitivity such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc as defined on page 18 of the specification.

The specification discloses in Table 14 on page 38 that treatment with polypeptides of SEQ ID NO: 4-6 delays the onset of EAE by 1 to 3 days where the EAE model is for early onset of multiple sclerosis, which is one of many autoimmune diseases. The EAE model used by Applicant is not appropriate for chronic relapse autoimmune disease, let alone for any other disease such as the ones recited in claim 134. Further, the experiments were not carried out long enough to see the effect of polypeptide of SEQ ID NO: 1 and 7 on chronic relapsing multiple sclerosis. In humans, the claimed autoimmune diseases encompassed by the claimed method are already established before therapy is offered. It is not clear that administering the claimed polypeptides shortly after (48 hours) or simultaneous given mouse spinal cord homogenate to induce acute onset of EAE accurately reflect on the chronic relapsing nature of autoimmune disease.

Van Noort et al teach the type of EAE induced is dependent on the immunization protocol, animal strain, and antigen used and some antigen used resulted in acute episode of EAE, others induce a chronic relapsing disease (See page 169, first full paragraph, in particular). Van Noort et al further teach that it is the chronic relapsing EAE that is reminiscent of multiple sclerosis (MS) because animals develop accumulating neurological features of the induced disease (See page 169. first full paragraph, in particular).

(2) Even if the method is limited to method of treating autoimmune disease by administering polypeptide selected from the group consisting of SEQ ID NO: 2, and 7, it is not clear that reliance on the EAE experimental model, which is a model for acute multiple sclerosis, accurately reflects on other autoimmune disease such as the ones recited in claims 134-142, especially Graft versus host disease, Host versus Graft disease associated with transplant or any delayed type hypersensitivity such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection. The EAE model is irrelevant to other disease such as rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis,

autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, much less Graft versus host disease, Host versus Graft disease associated with transplant or any delayed type hypersensitivity such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc

Van Noort et al teach experimental allergic encephalomyelitis (EAE) is only a model for multiple sclerosis and the EAE model is not appropriate for other autoimmune diseases such as rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity (See page 167 bridging page 168, Table III, in particular). Further, there is no guidance and working example demonstrating that any of the polypeptide such as SEQ ID NO: 1-7 could treat, much less could prevent any disease mentioned above.

(3) Even if the method is limited to treating multiple sclerosis, the specification on page 38 discloses that only two (SEQ ID NO: 2 and 7) out of seven polypeptides that could block EAE. However, the method of treating EAE with polypeptides of SEQ ID NO: 4, 5 or 6 delays the onset of disease with varying degree of blocking while polypeptides of SEQ ID NO: 1 and 3 have no in vivo data.

Pender *et al* teach that many therapies that are effective in the animal model such as experimental autoimmune encephalomyelitis (EAE), are either ineffective in MS or in the case of gamma interferon, lenercept and altered peptide ligands actually make multiple sclerosis (MS) worse (See abstract, in particular).

Given the infinite number of autoimmune disease, the limited working example and the unpredictable nature of the polypeptide even for just multiple sclerosis, a person of skill in the art could not predict which particular amino acid sequences of the claimed polypeptides are effective for treating EAE, let alone treating or preventing any autoimmune disease as encompassed by the claimed method.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 6/27/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) Table 14 shows that the mean score for the control was 4.9 on a 0-5 scale of disease severity, with 5 being the most severe, i.e. death. However, the mean scores for polypeptides of SEQ ID NO: 2, 4, 5, 6, and 7 were 0, 2.8, 0.2, .7, and 0, respectively. Applicants contend that amended claims 123 and 133 directed to a method of treating an autoimmune disease with polypeptides of SEQ ID NO: 2, 4-6 and 7 are enabled. (2) Table 4 demonstrates that 4 out of 10 mice treated with SEQ ID NO: 4 did not develop clinical symptoms of EAE and 7 out of 10 mice treated with SEQ ID NO: 6 did not show clinical symptoms of SEQ, while every control mouse exhibited clinical symptoms of EAE. The onset of EAE, at minimum, delayed beyond the conclusion of the experiment. Applicants contend that claims 152 and 157 directed to a method of delaying the onset of an autoimmune disease with polypeptides of SEQ ID NO: 2, 4-6, and 7 are enabled. (3) the term "preventing" in claims 123, 133, and 142 has been deleted. (4) EAE is a model for demyelinating disease, including Multiple Sclerosis as evidenced by Lisak et al (exhibit 55 of August 1, 2002). Applicants contend that the EAE is accepted in the scientific community as a model for multiple sclerosis. (5) Applicants point out that Aharoni et al states that suppressor cell activity has been shown in the EAE model in mice and rats and has been suggested in other autoimmune disease. (exhibit 110 of August 1, 2002), a copy of which is being submitted herewith. (6) Furthermore, copolymer 1 has been suggested for the treatment of autoimmune disease (Kipnis and Schwartz, Exhibit 6). The polypeptides of the subject invention as demonstrated on page 36, line 20 to page 37, line 22 of the subject specification, which shows that the polypeptides of the subject invention were recognized by monoclonal antibodies against Copolymer 1. Two out of four T cell lines specific

to copolymer 1 recognized the polypeptides of the subjection invention. (7) The WO 00/05250 teaches that Copolymer 1 is useful in the treatment and prevention of autoimmune disease and specifically lists all of the autoimmune disease enumerated in claim 134 of the subject specification. Example 6 of the publication shows that Coplymer 1 inhibits the proliferation of T cells specific to MBP, which has been suggested as an autoantigen in multiple sclerosis. (8) Allen Blacks (Exhibit 8) teaches DHT responses operate on the same principle as autoimmune response (proliferation and secretion of cytokines by T cells in response to an antigen). Applicants assert that the subject application also enables the treatment and prevention of host-versus-graft-disease (HVGD) and graft-versus-host-disease (GVHD). Schlegel et al discloses that GLAT, or Copolymer 1 is effective in the prevention of GVHD. A copy of Schegel et al may be found in Exhibit 132 of the August 1, 2002 IDS.

However, the claims still recite a method of treating a mammal afflicted with any autoimmune disease comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, 4, 5, 6 and 7 or a mixture of said purified polypeptides.

In response to item 2, although Table 4 demonstrates that 4 out of 10 mice treated with SEQ ID NO: 4 did not develop clinical symptoms of EAE and 7 out of 10 mice treated with SEQ ID NO: 6 did not show clinical symptoms of SEQ, while every control mouse exhibited clinical symptoms of EAE. The mean onset of EAE in mice treated with SEQ ID NO: 4 is 11.7 days, the mean onset of EAE in mice treated with SEQ ID NO: 6 is 12 days compared with the mean onset for the control is 11.3 days at the conclusion of the experiment.

In response to items 3-8, although the term "preventing" in claims 123, 133, and 142 has been deleted, the amended claims still encompass a method of treating any autoimmune disease or delaying the onset of any autoimmune disease. The specification discloses in Table 14 on page 38 that treatment with polypeptides of SEQ ID NO: 4-6 delays the onset of EAE by 1 to 3 days where the EAE model is for early onset of multiple sclerosis, which is one of many autoimmune diseases. Consistent with the teaching of Lisak et al, EAE is a model for multiple sclerosis and not for any autoimmune disease such as rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, graft versus host disease (GVHD), host versus graft disease

(HVGD) associated with transplant or any delayed type hypersensitivity such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc as defined on page 18 of the specification. There is no showing in the specification as filed that the claimed method could treat any other autoimmune diseases, including graft versus host disease (GVHD), host versus graft disease (HVGD) associated with transplant or any delayed type hypersensitivity such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc other than multiple sclerosis. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01. The objective evidence of record indicates that claimed method of treating a mammal afflicted with multiple sclerosis only comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, 4, 5, 6 and 7 or delaying the onset of multiple sclerosis comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, 5, and 7.

8. Claims 123-125, 127, 129-142, and 144-166 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treating *any* autoimmune disease, *any* B cell mediated autoimmune disease, or *any* T cell mediated autoimmune disease or any autoimmune disease such as the ones recited in claims 134 and 144, *any* graft versus host disease, *any* host versus graft disease, or *any* delayed type hypersensitivity in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7 or a mixture of purified polypeptides as set forth in claims 123-142, and 144-151; (2) a method of delaying the onset of any autoimmune disease, *any* B cell mediated autoimmune disease, or *any* T cell mediated autoimmune disease or any autoimmune disease such as the ones recited in claim 158, *any* graft versus host disease, *any* host versus graft disease, or *any* delayed type hypersensitivity in any mammal comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7 or a mixture of purified polypeptides as set forth in claims 152-166.

The specification discloses only a method for treating female (SJL/J x BALB/c) mice with mouse spinal cord homogenate to induce EAE, which is a model for multiple sclerosis and a polypeptide selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7. The results show in Table 14 that only polypeptides SEQ ID NO: 2, and 7 block the progression of EAE while treatment with polypeptides of SEQ ID NO: 4, 5 and 6 fail to block the progression of EAE (see page 38). In fact, treatment with polypeptides of SEQ ID NO: 4-6 does not prevent EAE because it has a mean onset of EAE at days 11.7, 14, and 12, respectively, as compared to control (11.3 days). The delayed onset of disease for polypeptides of SEQ ID NO: 4 and 6 is not significantly different than the control. Note, the block in the progression of disease is the treatment using polypeptides of SE QIDNO: 2 and 7 could simply due to a delay in the onset of EAE because there is insufficient information on the time course in the specification as filed, much less about relapse.

With the exception of the specific method of treating multiple sclerosis by administering the specific polypeptides mentioned above, there is insufficient written description about the method of *treating* or delaying the onset of any other autoimmune disease such as any B cell mediated autoimmune disease, any T cell mediated autoimmune disease, any demyelinating disease, any inflammatory disease, rheumatoid arthritis, osteoarthritis, autoimmune hemolytic anemia, autoimmune oophoritis, autoimmune thyroiditis, autoimmune uveoretinitis, Crohn's disease, chronic immune thrombocytopenic purpura, colitis, contact sensitivity disease, diabetes mellitus, idiopathic myxedema, myasthenia gravis, psoriasis, pemphigus vulgaris, or systemic lupus erythematosus, including graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity such as such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc as defined on page 18 of the specification comprising administering to the mammal a purified polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, 4, 5, 6 7 or a mixture thereof.

The specification discloses only a method of treating or delaying the onset of one autoimmune disease, which is multiple sclerosis by administering polypeptides selected from the group consisting of SEQ ID NO: 2, 4, 5, 6 and 7 using the EAE as a model for multiple sclerosis. Given the lack of a written description of *any* additional representative species of autoimmune diseases, including graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity such as such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc for the claimed method, one of

skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/27/03 have been fully considered but are not found persuasive.

Applicants' position is that the disease severity score in Table 14 on page 38 shows that polypeptides of SEQ ID NO: 2, and 4-7 treated EAE.

However, Base claims 123 and 133 encompass treating any autoimmune disease. Given the lack of a written description of *any* additional representative species of autoimmune diseases, including graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity such as such as poison ivy, poison oak or chemical contact, tuberculosis, leprosy, leishmaniasis, deep fungal infection, etc for the claimed method, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

9. The following new grounds of rejection are necessitated by the amendment filed 6/27/03.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 157-165 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "consisting essentially of" in Claim 157 represents a departure from the specification and the claims as originally filed. The passages pointed out by applicant in the amendment filed 6/27/03 do not provide a clear support for the said phrase.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 123-125, 127, 129-142, and 144-166 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "or a mixture of the purified polypeptides" in claims 123, 133, 142, 157 and 166 is ambiguous and indefinite because it is not clear which polypeptides in the mixture that applicants intend to claim. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
September 22, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600